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[1]Sh.A.Temirkulova, [2]A.A.Yessaliyev, [3]A.D. Nurmet
[1]International Kazakh-Turkish University named after Kh.A.Yassawi
[2]South Kazakhstan State University named after M.O. Auezov
[3]South Kazakhstan Medical Academy, Shymkent city

FEATURES OF THE TREATMENT OF ARTERIAL HYPERTENSION IN PREGNANCY (OVERVIEW)

The article reviewed the literature on the features of the treatment of hypertension in pregnant women. The goal of treating hypertension in pregnant women is the prevention of complications associated with an increase in blood pressure, the preservation of pregnancy, the normal development of the fetus and timely delivery. Before 12 weeks of gestation, a patient with hypertension before pregnancy should be examined to clarify the diagnosis, determine the functional state of the target organs, and decide on the possibility of prolonging the pregnancy.
Keywords: *hypertension in pregnancy, blood pressure, antihypertensive treatment, complications*

Arterial hypertension (AH) is a condition in which an SBP of ≥ 140 mmHg is recorded. and / or DBP ≥90 mm Hg as a result of repeated measurements of blood pressure, made at different times in a calm environment for the patient; however, the patient should not take drugs that affect blood pressure levels. To make a diagnosis of AH, it is necessary to confirm an increase in blood pressure by at least two measurements and for at least four hours [1,2,3].
Prevalence. AH during pregnancy is the most frequent extragenital pathology, it is diagnosed in 7–30% of pregnant women and serves as the main cause of deaths, perinatal mortality, significantly worsens the prognosis in the mother and in children. Complications of pregnancy with hypertension are: placental insufficiency; perinatal mortality; premature detachment of a normally located placenta; acute renal failure; acute heart failure; eclampsia, eclamptic coma; DIC syndrome; cerebral hemorrhage [4,5].
AH classification. Hypertensive conditions during pregnancy are represented by a group of diseases: - existing before pregnancy; - developed directly in connection with pregnancy. There are four main forms of hypertension: arterial hypertension before pregnancy (hypertension or symptomatic hypertension); gestational AH; AH, existing before pregnancy and combined with gestational hypertension and proteinuria; unclassifiable AH. AH in a pregnant woman in all cases contributes to the development of various complications of the mother and fetus. The greatest danger is PE (regardless of the level of blood pressure) and severe hypertension (blood pressure> 160/110 mm Hg). In these cases, the likelihood of development of detachment of a normally located placenta, rapid progression of hypertension with damage to target organs, such as the development of stroke in the mother, premature birth, or deceleration of intrauterine growth of the fetus increases dramatically. In moderate AH (140–159 / 90–109 mm Hg), clinical trials have not proven the benefit of AGT: there was no reduction in the risk of PE, perinatal mortality, premature birth, and low birth weight babies. However, the treatment of moderate hypertension prevents the development of severe hypertension [6,7,9,10].
The goal of treating hypertension in pregnant women is the prevention of complications associated with an increase in blood pressure, the preservation of pregnancy, the normal development of the fetus and timely delivery. Before 12 weeks of gestation, a patient with hypertension before pregnancy should be examined to clarify the diagnosis, determine the functional state of the target organs, and decide on the possibility of prolonging the pregnancy. Examination can be carried out both in a hospital, and out-patient, including, in the conditions of a day hospital [3,4,5].
Non-drug treatments. Measures for non-drug reduction of blood pressure should be recommended to all patients, regardless of the severity of hypertension and drug therapy: cessation of smoking; normal balanced diet without limiting the consumption of table salt and fluids; moderate aerobic exercise (FN), sufficient 8–10 hours of sleep at night, preferably 1–2 hours of sleep; reducing BM during pregnancy is not recommended due to the risk of low birth weight babies and subsequent slowdown in their growth. However, maternal obesity can cause adverse outcomes for both the woman and the fetus, therefore, recommended ranges of weight gain during pregnancy have been proposed [8,9,10,11]. According to the recommendations of the European Society of Cardiology for the treatment of cardiovascular diseases in pregnant women (2011) in patients with normal BMI (<25 kg/m^2), the recommended weight gain is 11.2–15.9 kg, in overweight women (25.0– 29.9 kg/m^2) - 6.8–11.2 kg, in women with obesity (> 30 kg/m^2) - <6.8 kg/m^2.
Drug therapy. Criteria for the onset of AHT in different variants of the course of AH in pregnant women are presented in Table 1.
The general principles of medical treatment of hypertension are:
• Maximum effectiveness for the mother and safety for the fetus.
• Start treatment with minimal doses of a single drug.

Table 1 - Criteria for initiating antihypertensive therapy with different options for hypertension in pregnant women

Clinical Options of AH	Blood pressure level, mm Hg
AH, before pregnancy without POM, AKS	>150/95
AG, available before pregnancy with POM, AKS	>140/90
Gestational hypertension	>140/90
Pre-eclampsia	>140/90

• Transition to another class of drugs with insufficient treatment effect (after increasing the dose of the first drug) or its poor tolerability.
• In the case of a woman taking AGP at the planning stage of pregnancy - correction of drug therapy: the abolition of angiotensin-converting enzyme inhibitors (ACE inhibitors), anigiotensin II receptor blockers and direct renin inhibitors, as well as the dose of the drug, achieving a target BP level <140/90 mm Hg.
• Use of long-acting drugs to achieve a 24-hour effect with a single dose. The use of such drugs provides a milder and more prolonged antihypertensive effect, more intensive protection of target organs, as well as high patient adherence to treatment.
Appointment during pregnancy of any drug must meet the safety requirements for the fetus, it is desirable that the drug does not have a negative effect on the physiological course of pregnancy and childbirth [11,12,13,14]. The FDA Food and Drug Administration (Food and Drug Administration) Classification of Food and Drug Administration identifies 5 categories of safety medicines for the fetus (Table 5). In accordance with the recommendations of VNOK (2010), the Working Group on the treatment of hypertension ESH, ESC (2007), as well as the recommendations of the European Society of Cardiology for the Treatment of Cardiovascular Diseases in Pregnant Women (2011), 3 groups are currently used to treat hypertension during pregnancy AhP meeting the criteria for pharmacotherapy during pregnancy:- drugs of central action (methyldopa);- calcium antagonists (AK) of the dihydropyridine series (long-acting nifedipine); - cardioselective β-blockers (β-AБ) (metoprolol succinate, bisoprolol).
Combined therapy is carried out in case of failure of monotherapy in the maximum dose. A rational combination is long-acting nifedipine + α-AB, with the ineffectiveness of such a combination, hydrochlorothiazide may be added in small doses (6.5–25.0 mg/day) [14,15,16].

The main drugs recommended for use during pregnancy for the treatment of hypertension are presented in Table 2. Acetylsalicylic acid in a low dose (75–100 mg /day) is used prophylactically in women with a history of early (<28 weeks) PE. Treatment begins before pregnancy or early pregnancy (up to 16 weeks of gestation) and continues until delivery [14,15,20].

Table 2 - Antihypertensive drugs recommended during pregnancy

Drug/ FDA category	Dose	Commentaries
Methyldopa (V)	from 0.5 to 3.0 g/day. 2-3 receptions	In terms of 16-20 weeks. pregnancy is not recommended due to its possible effect on fetal dopaminergic receptors. In the postpartum period, the use of methyldopa should be avoided, given the risk of developing postpartum depression.
Nifedipine (C)	from 30 to 180 mg/ day. slow release of the active substance	Causes tachycardia.
Cardio selective β-AB (C) (metoprolol succinate, bisoprolol)	depends on the drug	May reduce placental blood flow, in high doses increase the risk of neonatal hypoglycemia and myometrial tone.
Hydrochlorothiazide (C)	6.5 to 25.0 mg/day	Reduced BCC and hypokalemia may develop.

In the postpartum period, even in normotensive women, a tendency to an increase in blood pressure is observed, which reaches maximum values on the 5th day after birth, which is a consequence of the physiological increase in fluid volume and its mobilization into the vascular bed. In patients with hypertension, the same trend continues. The choice of drug in the postpartum period is largely determined by breastfeeding, but it is usually recommended the same drugs that a woman received during pregnancy and after childbirth. However, it should be emphasized that diuretics (furosemide, hydrochlorothiazide, spironolactones) can reduce milk production [16,17,18].

Treatment of AH during lactation. Controlled studies assessing the neonatal effects of AGP that the mother is taking are not currently available. It is known that milk secreted by alveolar cells is a suspension of fatty drops with a high content of proteins, the pH of which is <the pH of the mother's blood plasma. Factors contributing to the penetration of the drug into breast milk are: - small amount of milk; - weak binding to plasma proteins; - high solubility in lipids; - reduced physiological pH of milk.

The effect of the drug on a child depends on the amount of milk eaten, the interval between taking the drug and feeding, the characteristics of the pharmacokinetics and pharmacodynamics of the drug, and the child's ability to eliminate it. Neonatal effects when taking methyldopa during breastfeeding is considered safe. Atenolol and metoprolol accumulate in milk in a concentration that can have a negative effect on the child, while there is no such effect when usingpropranolol. In relation to such cardioselective β-AB, as bisoprolol, betaxolol, nebivolol, information about the neonatal effects of breastfeeding is currently not received [17,18,19]. Regarding the safety of an ACE inhibitor when breastfeeding information exists only about 2 drugs - captopril and enalapril. Currently, there are no data on the effect of ARBs on breastfeeding. Various animal tests show the negative effect of this group of drugs on the level of milk, as a result of which ARBs cannot be recommended for use during lactation. Diuretics (hydrochlorothiazide, furosemide and spironolactones) can reduce the formation of milk, but can be prescribed if necessary. AGP compatible with breastfeeding are recognized: methyldopa, nifedipine, verapamil, diltiazem, propranolol, oxprenolol, nadolol, timolol, hydralazine, hydrochlorothiazide, spironolactone, captopril, enalapril [20,21,22,23].

Tactics of management of patients with hypertensive crisis. The course of hypertension can be complicated by hypertensive crisis (CC). This is a rapid, additional, significant rise in blood pressure, which can be triggered by FN and mental stress, the intake of large amounts of salt, fluid, and the abolition of drug treatment. Increased blood pressure to 170/110 mm Hg requires urgent hospitalization and drug therapy. Emergency hospitalization of the woman is required, preferably in the intensive care unit in order to continuously monitor blood pressure and parenteral administration of AHD for a rapid decrease in blood pressure (Table 3).

Table 3 - Antihypertensive drugs for the treatment of hypertensive crisis

Drug	Dose	Beginning	Duration	Side effects	Special effects
Nitroglycerin (C)	5–15 mg/h e/v	5–10 min	15-30 min, may be > 4 h	Tachycardia, headache, facial flushing, phlebitis	The drug for preeclampsia complicated by pulmonary edema
Nifedipine (C)	10–30 mg per os, if necessary, within 45 minutes again	5–10 min	30–45 min	Tachycardia, headache, facial flushing,	Can't be taken sublingually and in conjunction with magnesium sulfate
Methyldopa (V)	0.25 mg, the maximum dose of 2 g during the day.	10–15 min	4–6 hours	May cause orthostatic hypotension, fluid retention, bradycardia	May mask fever in infectious diseases

In the treatment of acute hypertension, intravenous medication is safer and more preferable than oral or intramuscular (intramuscular) administration, since it can prevent the development of severe hypotension by stopping the infusion.

Blood pressure must be reduced by 25% from baseline during the first 2 hours and until its level is normalized in the next 2–6 hours. Gestational hypertension (GAH) treatment (after 20 weeks of gestation) is carried out in an obstetric hospital. When a good effect from treatment is obtained (normalization of blood pressure, lack of proteinuria, satisfactory condition of the mother and fetus), it can be continued on an outpatient basis, and if the therapy is insufficient, the pregnant woman is in the hospital until delivery [22,23]. Pregnant women who are observed on an outpatient basis should be hospitalized in an obstetric hospital 2-3 weeks before the expected time of delivery. In the hospital, after assessing the state of the mother and fetus, the method and time of delivery are selected. At all the above stages, a dynamic monitoring of the state of the placental complex, prevention and, if indicated, correction of the detected violations (according to the standards adopted in obstetrics) is carried out.

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[1]Ш.Ә.Теміркұлова, [2]А.А.Есалиев, [3]Ә.Д. Нұрмет

[1]Қожа Ахмет Ясауи атындағы Халықаралық қазақ-түрік университеті
[2]М.О. Әуезов атындағы Оңтүстік Қазақстан мемлекеттік университеті
[3]Оңтүстік Қазахстан медицина академиясы, Шымкент қаласы

ЖҮКТІ ӘЙЕЛДЕРДІҢ АРТЕРИЯЛЫҚ ГИПЕРТОНИЯСЫН ЕМДЕУ ЕРЕКШЕЛІКТЕРІ

Түйін: Мақалада жүкті әйелдердің гипертониясын емдеу ерекшеліктері туралы әдебиеттер қарастырылған. Жүкті әйелдердің гипертензиясын емдеу мақсаты артерия қысымын жоғарылатуын алдын алуы, жүктіліктің сақталуы, ұрықтың қалыпты дамуы және уақытында жеткізілуімен байланысты асқынуларды болдырмау болып табылады. Жүктіліктің алдындағы 12 аптадан бұрын жүктілікке дейінгі артериалды гипертониямен ауыратын науқас диагнозды анықтап, мақсатты мүшелердің функционалдық жағдайын анықтайды және жүктілікті ұзарту мүмкіндігін шешеді.
Түйінді сөздер: жүкті әйелдердің гипертониясы, қан қысымы, антигипертензивтік терапия, асқынулар.

[1]Ш.А. Темиркулова, [2]А.А.Есалиев, [3]А.Д. Нурмет

[1]Международный казахско-турецкий университет им. Ходжи Ахмеда Ясави
[2]Южно-Казахстанский государственный университет им. М.О. Ауезова
[3]Южно-Казахстанская медицинская академия, г.Шымкент

ОСОБЕННОСТИ ЛЕЧЕНИЯ АРТЕРИАЛЬНОЙ ГИПЕРТОНИИ У БЕРЕМЕННЫХ

Резюме: В статье проведен обзор литературы по особенностям лечения АГ у беременных. Целью лечения гипертонии у беременных является предотвращение осложнений, связанных с повышением артериального давления, сохранением беременности, нормальным развитием плода и своевременными родами. До 12 недель беременности пациент с гипертонией до беременности должен быть обследован, чтобы уточнить диагноз, определить функциональное состояние органов-мишеней и принять решение о возможности продления беременности.
Ключевые слова: гипертония у беременных, артериальное давление, антигипертензивная терапия, осложнения